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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,100	01/09/2006	Sarah C. Bodary	P1977R1	3801

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EXAMINER	
LEAVITT, MARIA GOMEZ	
ART UNIT	**PAPER NUMBER**
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,100	BODARY ET AL.	
	Examiner	Art Unit	
	Maria Leavitt	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *1-19, 23-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-22,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04-21-2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant response of 11-17-2006 has been entered. With regard to restriction requirements, Applicant election **without traverse** of Group X with respect to PRO71202, which corresponds to SEQ ID NO:1 and Group XV, claims 21 and 28, drawn to a method for diagnosing an immune related disease in a mammal by detecting the level of a gene encoding a PRO71202 is acknowledged. For the purpose of a compact prosecution, claims 20, 22 and 27 as they related to SEQ ID No. 1, drawn to a method for determining the presence of a PRO polypeptide in a sample, a method of diagnosing an immune related disease in a mammal with an anti-PRO71202, and a method of stimulating the immune response in a mammal, respectively will be rejoined with the elected groups. Claims 1-19 and 23-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected invention, there being no allowable generic or linking claim.

Therefore, Claims 20- 22, 27 and 28 are currently under examination to which the following grounds of rejection apply.

Priority

The current application filed on January 09, 2006 claims benefit of provisional application, 60/410,340 filed on September 11, 2002. However, as is detailed below in the 35 USC § 101 rejection, neither the present disclosure nor the provisional application support an enable utility, Accordingly, the application is given the priority date of 1-9-2006, which is the date of filing.

Information Disclosure Statement

The information disclosure statement filed February 21, 2006 has been considered. Please see the attached initialed PTO-1449s.

Specification

The Specification is objected because of the use of hyperlinks and other forms of browser-executable code. Some of the pages including hyperlinks are: p. 17, line 35; p. 28, line 11 and p. 36, line 11. 37 CFR 1.57(d) states that incorporation by reference by hyperlink or other form of browser executable code is not permitted. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See 37 CFR 1.57(d) and MPEP § 608.01(p)

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21 and 22, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21 and 22 refer to "immune related diseases". The as-filed specification does not disclose the meaning of the phrase "immune related diseases". The term "related" is a relative term subject to the artisans interpretation. On one hand, immune "related" diseases can be interpreted as autoimmune diseases, on the other, they can be interpreted as infectious diseases, cancer, or virtually every disease. As such, the metes and bounds of the claims cannot be determined.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 20, 21, 22, 27 and 28 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The applicant's elected invention is for PRO71202, which corresponds to SEQ ID NO: 1. The amendment to the original claims comprising the computer readable copy of the Sequence Listing entitled, " P1977R1" was filed on 01-09-2006, after the filing date of the Specification, date of filing 03-09-2005, including the sequences identified as SEQ ID NOs: 1-106. However, there is not disclosure in the as-filed specification as to the correlation of these sequences.

The specification contains some discussion in Figs. 3A-4C of differential emission intensity of wavelengths of the chromospheres of microarrays hybridized with probes synthesized from purified RNA in order to analyze actual gene expression in diseased colon tumor relative to healthy tissues (p. 36, 30-33, however, this is not enough to establish a specific and substantial utility.

Page 17, lines 16-21, teach that the invention is useful in the detection and quantification of gene expression in tissue samples providing a method of improving detection limit for gene expression in tissue samples.

However, the specification does not disclose what the activity of PRO71202, which corresponds to SEQ ID NO: 1 actually is. This does nothing to establish any nexus between the

unknown (or at least undisclosed) PRO71202 activity and a physiological effect on the subject. For example, the identification of compounds or agents that can be used to treat immune related disorders characterized by (or associated with) aberrant or abnormal PRO71202 expression and/or abnormal PRO71202 polypeptide activity might be scientifically interesting but no disorder is mentioned nor is any disorder shown to be characterized by or associated with PRO71202 polypeptide.

Similarly, use of an anti-PRO71202 antibody in a method of diagnosing an immune related disease in a mammal may be scientifically interesting but there is no disclosure of what exactly such an anti-PRO71202 antibody might be used for other than to treat some unknown (or at least undisclosed) immune related diseases. Figures 1-4 do not help establish a utility since they contain no disclosure of what PRO71202 polypeptide's function actually is.

Also, use of PRO71202 polypeptide in a sample suspected of containing said polypeptide does not constitute a specific and substantial utility in the absence of a disclosure of what the sample composition is supposed to diagnose.

Figs. 3A-4C come closest to establishing a utility but it, too, falls short. The example demonstrates that "a comparison of gene expression in colon tumor relatively to gene expression in the control tissue comprising pooled epithelia". However, there is no disclosure of what the function of the PRO71202 might be and certainly no evidence that differential expression of PRO71202 is related to a method of diagnosing cancer, let alone an immune related disorder.

The initial burden of establishing a lack of utility belongs to the examiner; the above discussion fulfills that burden.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20, 21, 22, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not provide an enabling disclosure for determining the diagnosis of immune related diseases by measuring the level of a gene encoding PRO71202 alone and/or expression of a PRO71202 polypeptide. The specification merely teaches a comparison of the level of gene markers from a sample in colon tumor relative to gene expression in the control tissue. There is not disclosure of the correlation of PRO71202, which corresponds to SEQ ID NO: 1, with detection of the probes hybridized to the array, said probes synthesized from 200 pg, 20 pg and 2 pg with only one round of amplification by cRNA reverse transcription (p. 36, lines 33-35).

The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to use the invention commensurate in scope with this claim. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims, when given the broadest possible interpretation, encompass a method for diagnosing an immune related disease by merely comparing levels of a marker gene expression in a specimen of colon tumor or ovarian carcinoma cell line in relation to control tissue comprising pooled epithelial tissue and do not indicated how any detected changes in expression level of a gene encoding PRO71202 and/or presence of a PRO71202 polypeptide reflects on the efficacy of the diagnosis. The specification provides insufficient data to enable claims directed to the method as broadly claimed. Thereby, specific issues including expression profiles of gene markers in colon cancer tissues as related to non-cancerous colonic epithelium and correlation of a gene encoding PRO71202 have to be examined and considered for patentability regarding the broadly claimed methods of diagnosing immune related disease in a patient.

The instant specification discloses in Example 6, on pages 35 and 36, extraction of total RNA from tumor cells microdissected from tumor tissue (e.g., colon tumor or ovarian carcinoma cell lines) used for synthesis of probes hybridized to a microarray (p. 36, lines 20-35). Target polynucleotides are attached to silanized slides that have been cross-linked using a bifuntional cross-linking agent (i.e., PDITC) able of reacting with silane on the glass slide at one end and with amino-derived microrarray DNA at the other end, thus firmly attaching microarray DNA to the glass surface (p. 30, lines 11-15). However, the as-filed specification is silent about any differential upregulation or downregulation of colon tumor markers from a patient or ovarian

carcinoma cell lines as compared to control samples. It is also unclear whether control samples are from the same cancer donor or different donors (p. 10, lines 5-11). Moreover, the specification fails to disclose in Example 6 how the level of a gene encoding PRO71202 is modified in relation to the expression level in a normal sample and thus the patient is judged to be affected with an immune related disease, the specification does not provide any reference level for the expression of a gene encoding PRO71202 in any of the normal tissues. Even assuming that a gene encoding PRO71202 is expressed in microarrays hybridized with probes synthesized from a colon tumor and its level is modified in relation to the level from normal epithelium from the same patient there is not teaching to the relative level of alteration of said gene in any other tissue other than colon tumors and correlated normal colon tissue. Further there is of teaching to the relative upregulation or downregulation of said gene. Thus, the teachings of the specification, while broadly suggesting microarrays hybridized with probes synthesized from colon tumors, only provides evidences for determining diagnosis of a colon cancer patients by comparing in the same patient expression of gene markers in cancer tumor and corresponding normal colon mucosae (Figs 2C and 2D). Further, no correlation of a gene encoding PRO71202 and diagnosis of colon carcinoma is discussed, let alone correlation of a gene encoding PRO71202 and diagnosis of an immune related disease.

At the time of filing, a variety of biomarkers for tumors had been identified. However, the skilled artisan was aware that tumors arising form different tissues express different sets of biomarkers. Moreover, analysis of gene-expression at various stages of a particular cancer, e.g., colon cancer will vary. For example, Sinicrope et al., (1999, Clin. Can. Res. Vol. 5, 1793-1804) teaches that the lack of diagnostic value of p53 expression on survival in colon carcinoma is

dependent on the stage of the tumor, citing the work of Ahnen et al., who demonstrated that while p53 staining is not diagnosis for stage II colon carcinoma, it does have diagnostic benefits for stage III colon carcinoma (Sinicrompe et al., p. 1801, col. 1). Lin et al., (2002, Oncogene, pages 4120-4128) bring similar insight into the unpredictability of using gene markers as a diagnostic tool when they teach that " the scoring system [molecular diagnosis score] must be validated using bulk tumors before it can become a tool for clinical diagnosis" (p. 4126, col. 2). Thus, the prior art demonstrates that the diagnostic value of any particular marker depends on the tumor type and the stage of the tumors.

In so far as using a gene encoding PRO71202 which corresponds to SEQ ID No. 1 in a method of diagnosis an immune related disease, Loring et al., (US Patent 6,682,888) teaches the same sequence cDNA as SEQ ID No. 43 (p. 89), that is 99.9% similar and a query match of 99.2% to the nucleotide of SEQ ID No. 1 of the instant invention. SEQ ID No. 43 is used in a composition useful for diagnosing or treating subjects with Alzheimer's disease. Specifically, the author discloses that SEQ ID No. 43 is down regulated at least two folds in the brain of subjects with Alzheimer's disease (see SCORE search results details for application 10527100_1, rng, Result 3). It is noted that Alzheimer's disease is a neurodegenerative disorder consisting principally of nerual loss or atrophy.

As set forth above by the nature of the invention, the state of the prior art, neither the prior art of record nor the as-filed specification provides sufficient guidance to enable a person skilled in the art to employ a method for diagnosis an immune related disease in a mammal by the establishment of level of expression of a gene encoding PRO71202 and/polypeptide as a diagnostic tool for immune related diseases. As the result, given the unpredictability of the art

and the lack of working example in the instant specification, particularly when taken with the lack of guidance in the specification, it would have required undue experimentation to practice the instant method to identify an enormous number of methods as broadly or generically claimed, with a resultant identification of a method of diagnosing immune related disease with a gene encoding a PRO71202 in a mammal as broadly claimed.

Claim Rejections - 35 USC § 102(b)

Claims 20, 20, 22, 27 and 28 are drawn to methods for determining the diagnosis of immune related diseases by measuring the level of a gene encoding PRO71202 alone and/or expression of a PRO71202 polypeptide in a test sample of tissue cells by contacting with an anti-PRP71202 antibody. To the extend that the claims embrace a method for detecting the presence of a PRO71202 polypeptide by contacting with anti- PRO71202 antiboy, the following rejection apply.

The following is a quotation of the appropriated paragraphs of 35 U.S.C. 102 that forms the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20, 20, 22, 27 and 28 are rejected under 435 U.S.C. 102(b) as being anticipated by Loring et al., US 6,682,888, Date of publication Jan 27, 2004 (see SCORE search results details for application 10527100_1, rng, Result 3").

Loring et al., disclose a novel human diagnostic cDNA of SEQ ID No. 43 having 99.9% similarity and a query match of 99.2% to the nucleotide of SEQ ID No. 1 of the instant invention and methods for producing specific antibodies using said cDNA for the diagnosis of pathologic disorders characterized by abnormal expression of the protein encoded by the cDNA of SEQ ID No. 43 (col. 3, lines 61-67) . Specifically, Loring et al., teach that antibodies produced using the proteins of the invention are useful for the diagnosis of prepathologic disorders as well as the diagnosis of chronic or acute diseases characterized by abnormalities in the expression, amount, or distribution of the protein (col. 13, line 45-65). Moreover, Loring et al., teach a number of biochemical assays wherein antibodies can be used for detection of the protein encoded by the nucleotide of SEQ ID No. 43 including binding assays (col. 13, lines 28-36), immunoassays (col. 14, lines 1-5), ELISA, RIA, and fluorescent activated cell sorting (FACS)(col. 16, lines 7-19).

Thus, Loring et al., teach all the claimed limitations and anticipates Applicant's claimed invention

Conclusion

Claims 20, 21, 22, 27 and 28 are not allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding his application should be directed to Group Art Unit 1636; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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